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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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08/16/2001

Juan Yguerabide

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07/21/2006

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EXAMINER

YANG, NELSON C

ART UNIT PAPER NUMBER

1641

DATE MAILED: 07/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/932,128

Applicant(s)

YGUERABIDE ET AL.

Examiner

Nelson Yang

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 19 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 49-52, 55, 63, 66, 68, 71-73, 76, 80, 84 and 166-181 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 49-52, 55, 63, 66, 68, 71-73, 76, 80, 84, 166-173 and 176-181 is/are rejected.
- 7) ☐ Claim(s) 174 and 175 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 19, 2006 has been entered.

### ***Response to Amendment***

2. Applicant's amendment of claim 49, 174, 175, 179, and 181 is acknowledged and has been entered.
3. Applicant's cancellation of claims 60-62, 88, is acknowledged and has been entered.
4. Claims 49-52, 55, 63, 66, 68, 71-73, 76, 80, 84, 166-181 are currently pending.

### ***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 49-52, 55, 63, 66, 68, 71-73, 76, 80, 84, 166-179 are rejected under 35 U.S.C. 103(a) as being unpatentable over Margel [US 4,624,923] in view of Rembaum et al [US 4,929,400].

With respect to claim 49, Margel teaches teaches different subpopulations of monodisperse “alkaline” polyacrolein microspheres coated with gold (column 10, example 1), having diameters of 0.1  $\mu$ , 5  $\mu$ , and 0.4  $\mu$  (column 10, example 3). Margel further teaches that the microspheres may have bound anti-human chorionic gonadotropin antibody (column 9, lines 1-10). Although Margel teaches that the microspheres are monodisperse, Margel does not explicitly teach that they have a coefficient of variation in size of less than 5%.

Rembaum et al, however, teach microspheres comprising materials such as silver, gold, and polyHEMA and having precise size range with diameters below 1000 Angstroms (column 8, lines 41-54, lines 55-69), varying no more than plus or minus 1% (column 3, lines 65-68), and having covalent functional groups for further reaction and attachment to other materials such as antibodies or proteins (column 3, lines 50-55). Rembaum et al further teach that uniformly sized, small microsphere of the order of 100 Angstroms to 10 microns in diameter are preferred as carriers for biological substances such as antigens or antibodies, and that they provide monodispersity and result in less non-specific binding to the surface of cells or containers (column 2, lines 60-67).

Therefore, it would have been obvious for the microspheres of Margel to have precise size ranges varying no more than plus or minus 1%, as they are preferred as carriers for biological substances such as antigens or antibodies, as well as providing monodispersity and result in less non-specific binding to the surface of cells or containers.

7. With respect to claims 50-52, Margel teaches anti-human chorionic gonadotropin antibody bound to the microspheres (column 9, lines 1-10), which are both proteins and biopolymers. Rembaum et al also teach microspheres created from polymers, proteins (column 3,

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lines 40-45). Although neither Margel nor Rembaum et al specifically recite that proteins do not significantly interact with light in the visible region of the spectrum, this property is inherent in proteins, and therefore would be anticipated by Margel and Rembaum.

8. With respect to claims 55, Rembaum et al teach microspheres (column 3, lines 40-45) that are spheroid in shape (column 3, lines 60-63).

9. With respect to claim 63, Margel teaches a metal-containing polyaldehyde micropshere composed of a polyaldehyde microsphere to which a transient metal is bound (column 4, liens 12-16). Rembaum et al teach microspheres created from polymers, proteins, waxes, starches, glasses and metals (column 3, lines 40-45), and further comprising materials such as silver, gold, and polyHEMA and having precise size range with diameters below 1000 Angstroms (column 8, lines 41-54, lines 55-69).

10. With respect to claim 66, Margel teaches a metal-containing polyaldehyde micropshere composed of a polyaldehyde microsphere to which a transient metal is bound (column 4, liens 12-16). Rembaum et al teach microspheres created from polymers, proteins, waxes, starches, glasses and metals (column 3, lines 40-45), and further comprising materials such as silver, gold, and polyHEMA and having precise size range with diameters below 1000 Angstroms (column 8, lines 41-54, lines 55-69).

11. With respect to claims 68, Margel teaches a metal-containing polyaldehyde micropshere composed of a polyaldehyde microsphere to which a transient metal is bound (column 4, liens 12-16). Rembaum et al teach microspheres created from polymers, proteins, waxes, starches, glasses and metals (column 3, lines 40-45), and further comprising materials such as silver, gold,

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and polyHEMA and having precise size range with diameters below 1000 Angstroms (column 8, lines 41-54, lines 55-69).

12. With respect to claims 71-73, Margel teaches that the metal bound to the microspheres may be magnetic (column 2, lines 20-25). Rembaum et al teach that magnetic fillers can be incorporated into the particles used to form the microspheres (column 3, lines 45-50).

13. With respect to claims 76, 80, 84, Margel teach polyaldehyde microspheres coated with silver or gold (column 2, lines 15-30), where the sizes of the populations include 0.4  $\mu$ , 0.1  $\mu$ , 0.05  $\mu$  diameters (column 11-13, examples 8-25). Rembaum et al teach microspheres created from polymers, proteins, waxes, starches, glasses and metals (column 3, lines 40-45), and further comprising materials such as silver, gold, and polyHEMA and having precise size range with diameters below 1000 Angstroms (column 8, lines 41-54, lines 55-69).

14. With respect to claims 166, 168, 172, Margel teaches populations of polyaldehyde microspheres coated with silver or gold (column 2, lines 15-30), where the sizes of the populations include 0.4  $\mu$ , 0.1  $\mu$ , 0.05  $\mu$  diameters (column 11-13, examples 8-25), and further comprising a drug, antibody, antigen, enzyme or other protein (claim 7).

15. With respect to claim 167, Margel teaches microspheres comprising silver, palladium and platinum that result in black color changes, as well as microspheres comprising gold that result in purple color changes (column 6, lines 11-30).

16. With respect to claims 169-171, Margel teaches teaches different subpopulations of monodisperse "alkaline" polyacrolein microspheres coated with gold (column 10, example 1), having diameters of 0.1  $\mu$ , 5  $\mu$ , and 0.4  $\mu$  (column 10, example 3). Margel further teaches that the microspheres may have bound anti-human chorionic gonadotropin antibody (column 9, lines 1-

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10). Rembaum et al also teach microspheres created from polymers, proteins, waxes, starches, glasses and metals (column 3, lines 40-45).

17. With respect to claim 173, Margel teaches microspheres having diameters of 0.1  $\mu$  (column 10, example 3). Rembaum et al teach microspheres having precise size range with diameters below 1000 Angstroms (column 8, lines 41-54, lines 55-69).

18. With respect to claims 176, 178, Margel teaches microspheres having diameters of 0.1  $\mu$  (column 10, example 3) with bound anti-human chorionic gonadotropin antibody (column 9, lines 1-10).

19. With respect to claims 177, 179, Margel teaches microspheres having diameters of 0.1  $\mu$  (column 10, example 3) with bound anti-human chorionic gonadotropin antibody (column 9, lines 1-10). Rembaum et al also teach microspheres created from polymers, proteins, waxes, starches, glasses and metals (column 3, lines 40-45), and further comprising materials such as silver, gold, and polyHEMA and having precise size range with diameters below 1000 Angstroms (column 8, lines 41-54, lines 55-69).

20. Claims 180, 181 is rejected under 35 U.S.C. 103(a) as being unpatentable over Margel [US 4,624,934] in view of Rembaum et al [US 4,929,400], and further in view of Tarcha et al [US 5,567,628].

Margel discloses populations of polyaldehyde microspheres coated with silver or gold and further comprising antibodies. Margel fails to teach that the antibodies are anti-biotin, anti-fluorescein or anti-digoxinin antibodies.

Tarcha et al, however teach the use of anti-biotin antibodies as a means for attaching biotinylated antibodies (column 23, lines 20-45).

Therefore it would have been obvious in the invention of Margel and Rembaum et al to have microspheres comprising anti-biotin antibodies, as suggested by Tarcha et al, in order to attach biotinylated antibodies.

### ***Response to Arguments***

21. Applicant's arguments, see p.9-11, filed May 19, 2006, with respect to the rejections under 35 U.S.C. 103(a) with respect to claims 174, 175 have been fully considered and are persuasive. The rejection of claims 174,175 under 35 U.S.C. 103(a) has been withdrawn.

### ***Allowable Subject Matter***

Claims 174-175 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

### ***Conclusion***

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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23. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nelson Yang  
Patent Examiner  
Art Unit 1641

  
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